



The impact of pandemic influenza, with special reference to 1918

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Abstract

Pandemic influenza, by definition, affects the overwhelming majority of countries and population subgroups in the world in a very short period of time. The impact of pandemics is not merely a matter of the biology of the particular virus in individuals. Pandemics are a social phenomenon affected by prevailing social circumstances, e.g., war, economic conditions, crowding, and food supply. In turn, pandemics affect social organization and events, e.g., governance and famine. Much of the study of pandemic influenza has been in industrialized countries in temperate zones; the occurrence of excess morbidity and mortality, and the strain on health care and other services in these countries are well known. A conference in 1998 brought together an increasingly large body of historical research about the pandemic of “Spanish influenza” in 1918–1919. It included interesting contributions about the impact of the pandemic in areas such as sub-Saharan Africa, India (where mortality is estimated at 17 million, or about half the world total), and the Pacific Islands. There are important lessons for contemporary society from the impact of the pandemic of 1918–1919 and other pandemics. One can make a compelling case for pandemic preparedness, including developing and executing strategies both to prevent and to ameliorate pandemic spread. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Pandemic influenza; Impact; History; Pandemic preparedness; “Spanish influenza”

1. Introduction

In a short period of time, weeks to months, influenza pandemics wreak destruction throughout the world, causing enormous numbers of illnesses and staggering numbers of deaths. In a few months of 1918 and 1919, approximately 30 million people died. In India

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alone, the influenza pandemic of 1918, interacting with famine, is now believed to have taken the lives of 17 million persons [1]. Gina Kolata, in her recent book, “Flu”, makes the following observations on the worldwide impact of the 1918 pandemic: “In comparison, AIDS had killed 11.7 million people through 1997. World War I was responsible for 9.2 million combat deaths. . . World War II for 15.9 million combat deaths. Historian (Alfred) Crosby remarks that whatever the exact number felled by the 1918 flu, one thing is indisputable: the virus ‘killed more humans than any other disease in a period of similar duration in the history of the world’ [2].”

It is easy to characterize the pandemic of 1918 as an extremely unusual event and believe that nothing like it will ever occur again. It is much more appropriate, however, to consider pandemic influenza in relation to large storms, such as hurricanes, or earthquakes, or volcanic eruptions. In short, pandemic influenza, even of the magnitude of 1918, is an event that is likely to occur again. We just do not know when.

In this paper, we shall examine some of the attributes of pandemic influenza, its effect on individuals and on societies, and why these effects make a compelling case for pandemic preparedness, particularly planning to prevent or ameliorate pandemic spread.

2. Definition of pandemic influenza

There has not been a constant definition of the terms “pandemic influenza” or “influenza pandemics” over time. One type of definition is strictly epidemiologic: some use the term simply to refer to apparent worldwide spread of influenza epidemics. With this use of the term, it is possible to have “pandemics” of influenza every few years and to speak of the degree to which they are associated with severe illnesses or deaths. Others use the term to refer to worldwide spread of severe epidemics, ones associated with high rates of illness, complications such as pneumonia, and death. Even with this use of the term, it is possible to have “pandemics” of influenza every few years. More recently, the term has been used to refer to a combination of an epidemiologic and a virologic event. Thus, some use the term to refer to worldwide spread of severe epidemics in association with an antigenic shift in at least the hemagglutinin of the prevailing influenza A viruses. Finally, when there is an antigenic shift, it has been common for multiple waves of illness and deaths in the same “influenza season” to occur in at least some geographic locations. It also is common to see multiple epidemics in a couple of years period before there is significant antigenic drift in the newly shifted virus. Some use the term “influenza pandemic” to refer to the first major occurrence of the newly shifted virus (e.g., the Asian influenza pandemic of 1957), or to the first season of the newly shifted virus (e.g., the Asian influenza pandemic of 1957–1958), or to the period before there was significant antigenic drift (e.g., the Asian influenza pandemic of 1957–1959).

For the purposes of this paper, I shall use the term “influenza pandemic” to refer to unusually extensive and severe epidemics of influenza A, compared to recent experience with influenza, with the epidemics occurring throughout the world, in association with a major antigenic shift in at least the hemagglutinin. I shall generally confine the use of the term to either the first major occurrence of the newly shifted virus or to the first influenza season in which it appeared. In my use of the term, by definition, “pandemic influenza”

must have a large impact on populations. Also, my use of the term leaves some question of how to characterize the “herald wave” that occurred in some places in the early months of 1918 and likely resulted in seeding the virus throughout much, though not all, of the world. This wave of illness, unnoticed in many areas, was significant enough in Spain to lead to the name “Spanish influenza” that then stuck to the pandemic when global illness began to occur in the later months of 1918.

With the definition I am using, there were three influenza pandemics in the 20th century: 1918–1919, 1957–1958, and 1968–1969. Deaths were greatest in 1918–1919, and least in 1968–1969. The first two were associated with a major shift in both the prevailing influenza A hemagglutinin and neuraminidase, whereas, only the hemagglutinin shifted in 1968. The last pandemic prior to 1918 was in 1890, and it, too, had enormous impact. The hemagglutinin of the virus responsible for the 1890 pandemic appears to have been related to the H3 hemagglutinin that appeared in 1968 [3]. Elderly persons in 1968 had pre-existing antibody against this hemagglutinin and appeared to be relatively protected [3]. That, and the fact that there was no shift in the neuraminidase in 1968, may have been related to the relatively lesser impact of the pandemic of 1968–1969 compared to 1957–1958. Interestingly, in 1977, another major shift in the influenza A virus appeared. The H1N1 strains that began to circulate then were virtually identical to strains that had circulated in the 1950s and much of the adult population had been exposed to and had antibody to similar strains. Though worldwide epidemics of the new H1N1 strains occurred (the so-called “Russian flu”), the severity of these epidemics was not great, even among younger persons; and by the definition I am using, we will not consider the appearance of these H1N1 strains to have been associated with an influenza pandemic.

3. What is special about influenza pandemics?

Influenza pandemics occur irregularly. When they occur, most of the population is susceptible to the newly shifted influenza A strain, so that attack rates can range as high as 40–50% of the population. Further, the infections tend to be associated with viral pneumonia, which can be fatal, and to predispose other infected persons to secondary bacterial pneumonias, which also can be fatal. In 1918, it was common for persons to go from being perfectly healthy to dying of primary viral pneumonia in a matter of a couple of days. Although some infected persons are asymptomatic and although many, indeed most, of the illnesses associated with an influenza pandemic are mild (symptoms occur but the person remains ambulatory) or moderate (require the ill person to go to bed), pandemics are nonetheless associated with large epidemics of emergency room visits, hospitalizations for pneumonia, and deaths, in most affected geographic areas. In just one hospital in Atlanta, GA, in the pandemic of 1968–1969, medical emergency clinic visits doubled, pneumonia admissions and deaths attributable to pneumonia and influenza increased about seven-fold [4]. This puts an enormous strain on the healthcare system; and the 1968–1969 pandemic had relatively low impact compared to 1957–1958 and 1918–1919. Furthermore, when so many persons become ill in such a short period of time, there are significant economic and social effects, which we shall discuss below.

3.1. The impact of influenza pandemics in the United States

First, however, it is worth noting that pandemics, as defined above, have somewhat different patterns of morbidity and mortality than interpandemic epidemics of influenza A, even very large interpandemic epidemics. Recently, Simonsen et al. [5] have shown that with the pandemics of 1918, 1957, and 1968, mortality in the United States was relatively higher for younger persons (<65) than with subsequent epidemics of influenza A viruses carrying the same hemagglutinin. In 1918, with the emergence of H1N1 influenza, there were approximately 550,000 excess pneumonia and influenza deaths in the United States, and almost half of all excess deaths occurred among persons aged 20–40 [6]. That, however, is only part of the story. In 1918, virtually 100% of excess deaths were in persons <65; whereas, by 1936–37, only about 60% of excess deaths were in persons <65; and, by 1943–44, only 30% of excess deaths were in persons <65. In the Asian influenza (H2N2) era, a similar pattern was observed, at a lesser order of magnitude. In 1957–1958, there were two waves of illness and excess deaths. Overall, total excess mortality for the season was about 65,000, and 36% of the excess deaths were in persons <65. By 1967–1968, with the last appearance of Asian influenza in the United States, there were an estimated 22,000 excess deaths; and only 4% were in persons <65. Finally, in the Hong Kong (H3N2) era, the first appearance in 1968–1969 was associated with total excess mortality of approximately 28,000 and pneumonia and influenza excess mortality of approximately 16,000, of which over 40% were in persons <65. Since 1982, the H3N2 epidemics in the United States have been accompanied by less than 10,000 excess deaths per year and less than 10% of those have been in persons <65.

What are the implications of these patterns of mortality? First, we have become used to the notion that the principal impact of influenza is on the elderly. Not only is that not necessarily true; but Simonsen's analyses suggest that in pandemics, even if the principal impact happens to be among older individuals, younger ones are disproportionately affected. In any pandemic, it is likely that the effect on younger persons will be noticeable; and, should there be a large total impact of the pandemic, which is quite possible, this could lead to a significant social effect. In short, the next major pandemic should affect disproportionately countries with younger populations; and, throughout the world, there will be epidemics of children plunged precipitously into single-parent families or orphaned!

Simonsen et al. [7] have also looked at the impact of influenza epidemics on hospitalizations by studying the years 1970–1995. Not surprisingly, patterns in hospitalization tend to be similar to patterns in excess mortality. This includes the fact that the greatest proportional hospitalization for persons <65 tends to occur in the earliest years after emergence of a pandemic strain and decline over the years. Thus, again, one would predict that a next pandemic would lead to a noticeable increase in hospitalizations for pneumonia and influenza among younger persons, not just the elderly.

It is easy to think that, at least in Western countries, our medical capability for treating pneumonia and influenza is much greater today than during the pandemics of the 20th century. We have more antibiotics and better intensive care units. But, such thinking does not take into account a couple of important facts. (1) A pandemic of 1918 proportions, occurring in the United States today, would potentially cause 1.5 million deaths and

several times that number of hospitalizations. The United States, with its emphasis on efficiency in hospital care, is unlikely to have a fraction of the intensive care capacity necessary to bring state-of-the art treatment to most of the persons who would need it. (2) Secondary bacterial pneumonias in patients with influenza are not necessarily curable with current therapy. The most common cause of secondary pneumonia has been pneumococcal; but higher case-fatality has been associated with pneumonias caused by *Staphylococcus aureus*, Group A beta hemolytic streptococci, and *Hemophilus influenzae*. Even when these organisms are exquisitely sensitive to available antibiotics, the infections can be fatal. In 1918, of course, there were no available antibiotics; but in 1957, penicillin-resistant staphylococci proved to be particularly problematic. Now, there is increasing resistance of pneumococci to penicillin, and staphylococci are increasing resistant to methicillin. In the next pandemic of influenza, secondary bacterial pneumonias could prove to be very difficult to treat with existing antibiotics.

Meltzer et al. [8] have evaluated the potential economic impact of a moderately large pandemic of influenza in the United States, with 89,000–207,000 deaths, 314,000–734,000 hospitalizations, and 18–42 million outpatient visits. Such an occurrence would have an economic impact of US\$71–166 billion, “excluding disruptions to commerce and society”. The latter, of course, would be enormous.

3.2. *The worldwide impact of influenza pandemics*

It is common to focus on the impact of influenza in Western countries, particularly those, such as the United States, where systematic information on mortality has been available for many years. Pandemics, by definition, have global impact, and it is important to consider some of the features of this impact, to the extent it can be estimated. Although, regrettably, there is very little information about the impact of the Asian and Hong Kong influenza pandemics throughout the world, over the years, historians have paid increasing attention to the 1918 pandemic.

Patterson and Pyle [1], the source of the modern estimate of 30 million deaths around the world in this pandemic, have tried to compile mortality figures by region and country. Despite what was mentioned above about the enormous impact of the pandemic in the United States, in Patterson and Pyle’s estimates, “the highest death rates are generally from Africa and Asia, and the lowest from North America, Australia, and Europe. Not surprisingly, poor populations suffered more than wealthier ones with better food and shelter. Differential access to health care probably also had some impact; there was no specific therapy for influenza or its complications, but supportive care was useful.” In their estimates, mortality ranged from about 5 per 1000 in Europe and North America, to about 9 per 1000 in Latin America, to about 15 per 1000 in Africa, to 20–34 per 1000 in Asia. As mentioned before, India appears to have had the highest mortality.

In 1998, Professor Howard Phillips, in the Department of History at the University of Cape Town, and Professor David Killingray organized a conference, entitled, “Reflections on the Spanish Flu Pandemic after 80 years: causes, course and consequences” (see <http://www.uct.ac.za/depts/history/conf.htm>). Papers presented at this conference painted a picture of the social impact of influenza that is seldom as vivid in the epidemiologic literature. For example, Ramanna [9] chronicled some of the measures taken to cope with

the pandemic in and around Bombay, including setting up special hospitals, organizing volunteer medical support and charitable collections, and providing ways for cremating the huge number who died. Wakimura [10] recorded the inter-relationship between famine and influenza in India. On the one hand, failure of the monsoon led to reduced crops and very high prices for food, with attendant increases in malnutrition, which increased the impact of influenza infection. On the other hand, after influenza began to occur, the high mortality disrupted agricultural activities and increased the impact of the famine.

Sub-Saharan Africa appears not to have been affected by the “herald wave” in the early months of 1918 [1]. Influenza arrived in the region by ship in about August, 1918, and spread largely by ship, river boat, and railway [11,12]. Although case-fatality was much less than it had been for plague in Senegal, overall mortality was considerably greater [11]. In Tanzania, owing to the very large number of deaths, many chiefs suspended the traditional funerals, a step not taken lightly. In a number of areas, as in India, there was again an interaction between influenza and famine. Social disruption was significant. As Musambachime pointed out, “Mining areas in Northern Rhodesia (Zambia), Katanga, Southern Rhodesia (Zimbabwe) and South Africa were closed and labor recruitment for these and other employment centers was suspended for 4 months between October 1918 and February 1919... Both missionaries and administrative officers were unable to tour outlying areas to collect taxes” [13].

Western Polynesia was also affected, for the most part severely, by the 1918 pandemic [14]. Many of the islands there adopted quarantine policies, as did other island nations such as Mauritius and Australia. These policies mostly delayed outbreaks, but occasionally avoided them. As Herda [14] points out, “Western Samoa, which did not close off its port suffered one of the world’s worst death rates from the pandemic, while American Samoa, about 50 km away, avoided the pandemic entirely due to a full and effective quarantine. Western Samoan anger and bitterness over the pandemic—both the circumstances of its entry as well as its management by the colonial administration—was deep and fueled the formation of a proto-independence movement, known as the Mau, in the 1920s”. The administrator, from New Zealand, was removed from his post.

Overall, despite the fragmentary history available to us from around the world of the impact of the pandemic of 1918, and despite the fact that there was much less impact of the pandemics of 1957 and 1968, it seems clear that these events can cause enormous demands on medical services and enormous costs. Key individuals may become incapacitated or die, literally changing the course of history (for example, Crosby [15] documents the possible effects that influenza had on the European peace process in late 1918 and 1919). Social disruption can occur from interrupted services, owing to massive illness among workers and from sudden deaths of parents. There are likely to be unpredictable consequences such as loss of confidence in a government’s ability to handle the situation.

4. What would be different now?

Overall, as one reviews the history of the 1918 pandemic, it is striking that the occurrence of disease, although global, affecting almost all countries and almost all sub-

populations within a country, most severely affected persons who were poor, lived in crowded conditions, or were affected by hunger, pregnancy, or other concurrent illnesses. These situations persist today, and it does not take much imagination to realize that the effect of an influenza pandemic today in some of the poorer parts of the world could be enormous. A predictable tragedy would occur in countries in which there are large numbers of HIV infected persons. Furthermore, we have already reviewed the fact that even in first-world countries, medical facilities and resources would probably not be adequate to blunt the impact of a newly shifted influenza A virus infecting a population.

By 1889–1890, transportation by steamships and railroads was sufficiently well developed to support “a truly worldwide pandemic” [16]. In the 21st century, there should be no transportation barrier to spreading a potential pandemic strain of influenza A throughout the world in a very short period of time.

Thus, the only difference between then and now is our growing understanding of influenza virology and our ability to consider preventing or ameliorating pandemic spread. There seem to be several possibilities for doing this. (1) First, there can and should be global surveillance for novel strains infecting humans. It requires global organization and financial support to have a tight and effective surveillance network. Nonetheless, it is possible that the identification of the H5N1 infections in Hong Kong and the eradication of the avian reservoir (chickens and ducks) that appeared to be related to those infections, was an example of prevention of the emergence of a pandemic strain. (2) There is evidence that persons who have had natural exposure to similar strains exhibit some protection later in life when a pandemic strain emerges [3]. An important question is whether some similar sort of protection might occur with prior immunization to prototypes of the influenza A hemagglutinins? In other words, could prior immunization ameliorate illness during a subsequent pandemic? Furthermore, if it could, what would be the optimal time to begin giving the vaccine (for example, in early childhood, so as possibly to induce the phenomenon of “original antigenic sin” that occurs with natural infection in childhood [17]) and should the vaccine be live or inactivated? This set of questions merits thought since there are only 14 influenza A hemagglutinin types, and it should be possible with current technology to develop polyvalent vaccines and give them periodically through life. (3) A related strategy would be developing vaccines for prototype strains of influenza A viruses carrying the various hemagglutinin types and stockpiling them for use when a potential pandemic emerged. Although this approach would avoid “unnecessary” immunization, it raises practical issues about manufacturing and maintaining stockpiles. (4) Since pandemics often consist of more than one wave in an influenza season, or lead to recurrent epidemics in the next year or two, with the emergence of a potential pandemic strain, countries should consider immediate production of a vaccine, even if it appears that it cannot be produced in time to prevent the first epidemic wave. (5) There are now several antivirals that are effective at preventing influenza infection or modifying illness when given early enough. A next pandemic could be ameliorated if it were possible to have sufficient supplies of one or more of these antivirals available. (6) Although secondary pneumococcal pneumonia is less lethal than some of the other secondary bacterial pneumonias, it is

the most common type of secondary bacterial pneumonia. Pneumococcal vaccination at the time of emergence of a potential pandemic influenza strain might ameliorate the impact of the pandemic.

All of the above merit serious consideration and form an agenda for pandemic planning and for research. I find it troublesome that with the currently available knowledge and technology, most of the above options are unlikely to make much of a difference for all but the most affluent nations. The impact of the next major pandemic, although great in affluent nations, is likely to be even greater in the poorest nations. The first option, increasing global surveillance, is within our technical grasp and is clearly a critical part of developing a global strategy for thwarting emerging pandemic strains. A second consideration of great importance is focusing on methods for rapid development and production of inexpensive influenza vaccines that might be used for the general population of the world.

References

- [1] K.D. Patterson, G.F. Pyle, The geography and mortality of the 1918 influenza pandemic, *Bull. Hist. Med.* 65 (1991) 4–21.
- [2] G. Kolata, *Flu: The Story of the Great Influenza Pandemic of 1918 and the Search for the Virus that Caused it*, Farrar, Straus and Giroux, New York, 1999, p. 330 (p. 7).
- [3] S.C. Schoenbaum, M.T. Coleman, W.R. Dowdle, S.R. Mostow, Epidemiology of influenza in the elderly: evidence of virus recycling, *Am. J. Epidemiol.* 103 (1976) 166–173.
- [4] S.W. Schwarzmann, J.L. Adler, R.J. Sullivan Jr., W.M. Marine, Bacterial pneumonia during the Hong Kong influenza epidemic of 1968–1969, *Arch. Intern. Med.* 127 (1971) 1037–1041.
- [5] L. Simonsen, M.J. Clarke, L.B. Schonberger, N.H. Arden, N.J. Cox, K. Fukuda, Pandemic versus epidemic influenza mortality: a pattern of changing age distribution, *J. Infect. Dis.* 178 (1998) 53–60.
- [6] S.D. Collins, Age and sex incidence of influenza and pneumonia morbidity and mortality in the epidemic of 1928–29 with comparative data for the epidemic of 1918–19, *Public Health Rep.* 33 (1931) 1909–1937.
- [7] L. Simonsen, K. Fukuda, L.B. Schonberger, N.J. Cox, The impact of influenza epidemics on hospitalizations, *J. Infect. Dis.* 181 (2000) 831–837.
- [8] M.I. Meltzer, N.J. Cox, K. Fukuda, The economic impact of pandemic influenza in the United States: priorities for intervention, *Emerging Infect. Dis.* 5 (1999) 659–671.
- [9] M. Ramanna, Coping with the influenza pandemic, 1918–1919: the Bombay experience, in: S. Phillip, D. Killingray (Eds.), *The Spanish Influenza Pandemic of 1918–19: New Perspectives*, Routledge, London (in press).
- [10] K. Wakimura, The Indian experience of influenza pandemic 1918–19: why the mortality was so huge?, in: S. Phillip, D. Killingray (Eds.), *The Spanish Influenza Pandemic of 1918–19: New Perspectives*, Routledge, London (in press).
- [11] M. Echenberg, The dog that did not bark: evidence for the 1918 influenza pandemic in Senegal, in: S. Phillip, D. Killingray (Eds.), *The Spanish Influenza Pandemic of 1918–19: New Perspectives*, Routledge, London (in press).
- [12] J.G. Ellison, A fierce hunger: tracing the impacts of the 1918–1919 influenza pandemic in southwest Tanzania, in: S. Phillip, D. Killingray (Eds.), *The Spanish Influenza Pandemic of 1918–19: New Perspectives*, Routledge, London (in press).
- [13] M.C. Musambachime, A great catastrophe: the blood of the dead soldiers is killing us: African reactions to the influenza pandemic of 1918/1919 in Northern Rhodesia (Zambia) and Nyasaland (Malawi), in: S. Phillip, D. Killingray (Eds.), *The Spanish Influenza Pandemic of 1918–19: New Perspectives*, Routledge, London (in press).
- [14] P.S. Herda, Disease and colonialism in the Pacific: the 1918 pandemic in Western Polynesia, in: S. Phillip,

- D. Killingray (Eds.), *The Spanish Influenza Pandemic of 1918–19: New Perspectives*, Routledge, London (in press).
- [15] A.W. Crosby Jr., *Epidemic and Peace*, 1918, Greenwood Press, Westport, CT, 1976, p. 337.
 - [16] K.D. Patterson, *Pandemic Influenza 1700–1900: A Study in Historical Epidemiology*, Rowman and Littlefield, Totawa, NJ, 1986, p. 118 (p. 3).
 - [17] T. Francis Jr., F.M. Davenport, A.V. Hennessy, A serologic recapitulation of human infection with different strains of influenza virus, *Trans. Assoc. Am. Physicians* 66 (1953) 231–239.